AR 201-12549616

ROBUST SUMMARY
ALKYL SULFIDE CATETGORY
CAS # 68511-50-2
HEALTH ELEMENTS: REPEATED DOSE TOXICITY

Test Substance	
CAS #	68511-50-2
Chemical Name	1-propene, 2-methyl-, sulfurized
Remarks	This substance is also referred to as methyl propene derivative in HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "Chemical Description of Alkyl Sulfide Category" in HERTG's Test Plan for Alkyl Sulfide Category.
Method	
Method/Guideline followed	comparable to OPPTS 870.3250
Test Type	Thirteen week dermal subchronic toxicity study
GLP (Y/N)	Y
Year (Study Performed)	1989
Species	Rat
Strain	Sprague Dawley (Tac:N[SD]fBR)
Route of administration	Dermal to shaved skin of backs
Duration of test	5 days/week for 13 weeks
Doses/concentration levels	Part 1:500 and 2000 mg/kg/day undiluted test material; 500 mg/kg/day diluted 50%w/v in 100" mineral oil base stock Part 2: 500, 250, 100, 50, 10 mg/kg/day diluted in mineral oil base stock at concentrations of 25, 10 and 5% w/v respectively 20 (10M,10F/group): 8 treatment groups,1 vehicle control,2 untreated controls
Sex	Male and Female
Exposure period	
Frequency of treatment	
Control group and treatment	1 vehicle control,2 untreated controls Vehicle: mineral oil (100" solvent refined naphthenic base stock) density 0.88 g/ml
Post exposure observation period	
Statistical methods	Analysis of Variance followed by multiple range tests, Serum chemistry and hematology data were evaluated using the F test for ANOVA and Student-Newman-Keuls multiple comparison test.
Remarks field for test conditions	Age at initiation: 7 weeks old following 2 weeks acclimation Study was designed to identify inherent toxicity of test material and to determine whether dilution in a mineral oil carrier would alter toxicity. Methyl propene derivative was applied to the clipped backs of groups of 20 Sprague Dawley rats (10M,10F) 5 days per week for 13 weeks at dose levels of 500 or 2000 mg/kg/day undiluted or diluted in 100" mineral oil at dose levels of 500, 250,100, 50 or 10 mg/kg/day on the

	same schedule. Rats were fitted with Elizabeth collars to minimize ingestion of test material, which was left uncovered on the skin. One vehicle and 2 untreated shaved control groups were included in the study. Assessments for toxic response included daily clinical observations, weekly skin irritation scoring, weekly body weights and terminal organ weights, hematology, serum chemistry and urinalysis at weeks 5 and 13, gross necropsy evaluations , sperm morphology, and histopathology at study termination.
Results	
Remarks	Male rats treated with methyl propene derivative for 13 weeks at dose levels 250 mg/kg/day gained less weight (15% less at study termination) than controls. Female weights were unaffected. At doses 250 mg/kg/day, both sexes had decreased levels of red blood cells and increased levels of neutrophils in circulation, increased spleen size and increased pigment and red pulp in the spleen. At doses 100 mg/kg/day, there was increased production of WBC in spleen and bone marrow. Mean liver to body weights were increased in male rats at dose levels 250 mg/kg and in female rats at 500 mg/kg/day. Male rats treated with undiluted test material at 500 or 2000 mg/kg/day had increased kidney weights correlated with dose-related increase in hyaline droplet formation indicative of light hydrocarbon nephropathy. Undiluted test material and dilutions at 25% (500 mg/kg, 250 mg/kg in Part 2) induced moderate to strong reaction in the skin, characterized by erythema, edema , increased thickness and stiffness; these effects were more severe in the 500 mg/kg (diluted50%w/v) Microscopically, hyperkeratosis, hyperplasia of sebaceous gland, increased mitosis in epidermis and dermal abscesses were observed. Virtually no irritation was observed in the vehicle control group or in dose groups of 100, 50, 10 mg/kg/day where dilutions were made at 10% or 5 %w/v. No effects on sperm motility or morphology were observed in rats treated with 2000 mg/kg/day. The relative weight increases in livers of higher dose animals of both sexes had no microscopic correlate and is considered an adaptive response to treatment. The increase in kidney weight and hyaline droplet formation in male rats is indicative of light hydrocarbon nephropathy, a condition considered by EPA to be specific to male rats and not predictive of comparable toxicity in humans.[a] Although many changes in hematology parameters can be associated with infections which can occur with severe skin irritation, increased dose related neutrophil production was observed in animals with minimal skin irritation and can be considered a direct effect of the test material.

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Conclusions	NOEL for systemic toxicity was 50 mg/kg/day dermal exposure for 13 weeks. The minimally irritating concentration of methyl propene derivative diluted in 100" mineral oil base stock is 10% (100, 50, 10 mg/kg/day)
Data Quality	Reliable without restrictions: Guideline based study performed in accordance with US GLPs.
References	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information). United States Environmental Protection Agency (EPA) 1991. Alpha 2 microglobulin: association with chemically induced renal toxicity and neoplasia in the male rat. P.85 In Risk Assessment Forum, U.S. Govt. Printing Office, Washington, DC
Other	Updated: 12-29-99